Petroleum HPV

201-15135

March 3, 2004

The Honorable Michael O. Leavitt, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Attention: Chemical Right-to-Know Program

Re: Response to Comments on the Lubricating Oil Basestocks Test Plan
HPV Consortium #

Dear Administrator Leavitt:

The Petroleum HPV Testing Group is a consortium representing 92 percent of the nation's petroleum refining capacity. The Group is made up of 70 member companies of the American Petroleum Institute (API), the National Petrochemical & Refiners Association (NPRA), the Gas Producers Association (GPA) and the Asphalt Institute. The Testing Group appreciates the comments it received on its Test Plan for Lubricating Oil Basestocks that was received by EPA on March 25, 2003 and posted on the Agency's ChemRTK website on April 4, 2003. The Environmental Protection Agency (EPA), Environmental Defense (ED) and the People for the Ethical Treatment of Animals (PETA) on behalf of several animal welfare organizations submitted comments on the Test Plan. The three sets of comments contained questions and observations that necessitate a response from the Testing Group. In the interest of communicating our intent with all interested stakeholders, the Testing Group is providing a revised Test Plan and Robust Summary for posting on the ChemRTK website. In addition, the two documents will also be posted on our website, www.petroleumhpv.org.

To summarize the major issues contained in the comments and the Testing Group's responses:

Category Definition

ED thought both the Test Plan and the Robust Summary were well written and addressed the required SIDS elements to the extent possible. ED did suggest the proposed category should be subdivided to facilitate analysis. However, PETA thought the "category should be expanded to cover a broader range of heavy-end hydrocarbon substances and combined with the waxes and related compounds category."

The Testing Group acknowledges that there are additional ways to structure the Lubricating Oil Basestocks HPV category, but the Group thinks each way would have its own strengths and weaknesses. The Testing Group does not believe any of the alternative category arrangements would result in better use of the existing data or a reduction in the amount of proposed testing. After much deliberation, the Group thinks our proposal to divide the current Lubricating Oil Basestocks category into three subcategories achieves not only the ED goal of facilitating analysis, but maximizes the use of existing data and minimizes the amount of proposed additional animal testing. As noted in response to comments on the Waxes HPV Test Plan, the Testing Group understands that the intent of the PETA suggestion is to ensure the inter-relationships of lubricating oil basestocks and waxes are considered in developing the individual test plans. The Testing Group acknowledges that the processing history, physico-chemical properties and potential toxicities of lubricating oil basestocks and waxes are closely related, i.e. highly refined materials in either category have very low acute/chronic toxicity. The Testing Group has taken these relationships into account when developing the

individual test plans for the two HPV categories. Consequently, the Testing Group continues to believe it has, in practice, achieved the goal PETA hoped to achieve with its suggestion of

combining the two categories, yet still achieved EPA's goal of providing meaningful information for hazard and risk evaluation.

EPA noted the names for two of the CAS numbers (64742-44-5 & 72623-84-8) provided in the test plan are inconsistent with the names listed in EPA's Substance Registry System (SRS) Data Base.

The test plan has been revised to reflect the SRS entries.

PETA suggested that reference to existing data on TPH (ATSDR 1995), Fuel Oils (ATSDR 1995) and Mineral oils (ATSDR 1997) be added to the test plan.

The Test Plan has been revised to include reference to the ATSDR Toxicological Profiles on TPH and Hydraulic fluids (Mineral Oils). Reference to the ATSDR Toxicological Profile on Fuel Oils is included in a separate API HPV test plan (Gas Oils).

PETA noted that the test plan does not include any analysis of human exposure to these compounds.

Since analysis of human exposures is not an HPV/SIDS endpoint, the Testing Group has only dealt with this issue in a general way, choosing to perform any proposed mammalian testing via routes of exposures that are among the primary routes of human exposures.

PETA believes that based on the information in this Test Plan, the Testing Group should revisit the Waxes and Related Substances Test Plan and eliminate the proposed animal testing included in that plan.

After careful review, the Testing Group decided not to revise the Waxes and Related Substances Test Plan. While sharing PETA's desire to minimize the number of animals used in testing, the Testing Group continues to believe the proposed testing is necessary to further characterize the toxicity of the category members.

<u>Category Justification.</u>

EPA found the health and ecological effects information presented in the Test Plan and Robust Summary did not adequately justify the category. EPA thought additional data for members of all three subcategories of base oils needed to be added to each of these sections in both the Test Plan and Robust Summary. The additional information would allow the Agency to test the hypothesis presented by the submitter that adverse human health effects for these materials are a function of the type and degree of chemical processing.

As stated in the Test Plan, the inverse correlation between degree of processing and mammalian health effects applied only to the distillate base oils. The Testing Group did not propose that this correlation held for the residual oils.

With regard to the distillate base oils (Unrefined/Mildly Refined and Highly/Severely Refined), the Testing Group believes research supporting the inverse correlation between potential carcinogenicity and mutagenicity and the degree of chemical processing are well known and have been accepted by the general scientific community and a number of regulatory agencies (Bingham et al., 1965, 1996, 1979; Chasey and McKee, 1993; Doak et al., 1983; Halder et al., 1984; IARC, 1984; Kane et al., 1984; McKee et al., 1989; Roy et al., 1988, 1996). Consequently, it was not the Testing Group's intent to include in this Test Plan and Robust Summary all the data that supports the correlation between degree of processing and these two endpoints.

Given that all the materials in the distillate base oil subcategories have relatively low acute mammalian toxicities, the Testing Group is not surprised that the "crude" endpoints measured in acute studies do not show a clear correlation between processing and toxicity. Because of the consistently low acute toxicities of these materials found in numerous studies, the Testing Group does not think it would be worthwhile to expend animals and resources developing additional acute toxicity data.

The Testing Group believes that when the entire data base on the repeat-dose toxicity of these materials, their components, and related materials is considered, the correlation between degree of processing and repeat-dose toxicity becomes clear. The Testing Group thinks the apparent lack of correlation in the current Test Plan is created by the fact that:

- **by design, the Robust Summary provides details on only one or two studies per endpoint and does not include all the data that supports this correlation, and**
- **the Severely refined base oils have been more extensively studied than the unrefined base oils, leading to a more detailed description of their potential adverse effects.**

The Testing Group did not propose that the same inverse correlation (degree of processing and adverse health effects) applied to the residual base oils subcategory. *In vitro* mutagenicity testing and carcinogenicity testing of residual oils has been negative, supporting the Testing Group's position that these materials lack biologically active components or these components are not bioavailable. The lack of bioavailabe components in the residual oils is not surprising, given that the oils consist of large and complex hydrocarbons having carbon numbers predominantly higher than C25, with average molecular weights of 700 and boiling above approximately 725 °F (400 °C). Some of the components of these residual base oils may boil as high as 1500 °F. The aromatics found in these high boiling residual oils are highly alkylated (paraffinic and naphthenic), the estimated number of aliphatic carbons ranging from 13 to 25. The studies being proposed for this subcategory of material will generate data that allows the Testing Group to test the hypothesis that the residual base oils lack of biological activity extends to the repeat-dose and reproductive/developmental toxicity and *in vivo* genotoxicity endpoints.

With regard to ecological effects, the Testing Group does not think a correlation exists between toxic effects and degree of processing. Rather, the existing aquatic toxicity data support the position that the low water solubility of the distillate and residual base oils limits their bioavailability and hence their potential toxicity. As with acute mammalian toxicity, the aquatic toxicity of all the category members is low, thus one would not expect to see any toxicity "trend" for any of the three category subgroups. The Testing Group believes that the aquatic toxicity data presented in the test plan represents the expected toxicity of all the category members thus lending justification for grouping the base oils as a category.

<u>Physicochemical Properties</u>

Boiling Point
EPA considered the data submitted for boiling point to be adequate for the purpose of the HPV Challenge Program, but asked the Testing Group to explain how representative data will be used to address data gaps for the remaining members of the category.

Additional discussion has been added to the Test Plan to describe the boiling points of the remaining category members.

Melting Point

EPA considered the data submitted for melting point to be adequate for the purpose of the HPV Challenge Program, but there was an inconsistency in the measured values given in the test plan, i.e. there is a large difference in the pour point data given in Table 2 for representative Unrefined and Severely Refined distillate base oils. EPA also asked that the Testing Group explain how representative data will be used to address data gaps for the remaining members of the category.

The Testing Group has reviewed the Test Plan and found no inconsistencies. The values reported in Table 2 reflect measured values for representative substances of distillate lubricating oil basestocks in the "Unrefined" and "Severely Refined" subgroups. The difference in pour point values is a function of the refining process, which removes specific hydrocarbon groups (e.g., aromatic hydrocarbons) from the original feedstock. While EPA believed the existing data to be adequate, the text in the test plan has been reorganized to better illustrate pour point data for the category subgroups.

Vapor Pressure
EPA requested the Testing Group " to provide data or estimates on enough chemicals to represent all category members". EPA also asked that the Testing Group include in the Test Plan an explanation of how representative data will be used to address data gaps for the remaining members of the category.

The Test Plan and the robust summary have been revised to include additional information in the form of ranges of estimated vapor pressures for various low and high molecular weight component hydrocarbon molecules contained in distillate and residual Lubricating Oil Basestocks. Further discussion has been included to describe the vapor pressure characteristics of these materials. Finally, additional details of the cited vapor pressure study have been brought forward to help clarify the study results and address the apparent discrepancy between the statement in the Test Plan that testing the vapor pressure of these substances is not necessary because the estimated vapor pressures are below the testing threshold of 1x10-5 Pa and the one measured vapor pressure value in the test plan is almost 20 times this value. Additional discussion describing the vapor pressures of the remaining category members has been included in the Test Plan.

Partition Coefficient
EPA requested the Testing Group include a written summary that would include details on: relevant measured data, estimation methods, structures used in the estimation, an explanation for not including C20-C50 streams, and the results of each estimation in robust summary format. EPA also asked that the Testing Group include in the Test Plan an explanation of how representative data will be used to address data gaps for the remaining members of the category.

The test plan and robust summary have been revised to more clearly describe estimated partition coefficient values for a range of hydrocarbon structures characteristic of distillate and residual lubricating oil basestocks. Additional discussion describing partition coefficients of the remaining category members has been included in the Test Plan.

Water solubility
EPA requested the Testing Group revise the robust summary to include details on the estimation methods, including structures used in the estimation, and the results of each estimation. The Agency also thought the Test Plan should be revised to include an explanation of how estimates will be assigned to other category members.

The robust summary has been revised to include details on water solubility. The representative hydrocarbon structures used in water solubility estimations have been identified and additional discussion provided to cover other members of the category.

<u>Environmental Fate</u>

Photodegradation
EPA noted that it could not verify the Testing Group's estimates since the Test Plan does not provide information on the structures used in estimating the range of the half-life values given in the robust summary. The Agency requested the robust summary be revised to provide information on the structures used in the estimations, and the results of each estimation. The Agency also recommended the robust summary be revised to account for the C20 – C50 compounds in these estimates. EPA also requested the Test Plan be revised to include an explanation of how representative data will be used to address data gaps for the remaining members of the category.

The robust summary has been revised to identify the hydrocarbon structures used in the photooxidation half-life estimates and provide additional estimates and/or discussion for other category members (e.g., C20 – C50 compounds). Additional discussion has been added to the Test Plan to describe the photodegradation of the remaining category members.

Biodegradation
EPA requested the Testing Group revise the Test Plan to indicate how data gaps for the remaining category members will be addressed.

The Test Plan has been revised to include additional discussion on the biodegradation of the remaining category members.

Transport and distribution (fugacity)
EPA recommended that EQC level III, rather than EQC level I, be used to develop this analysis. EPA also asked that the robust summary be revised to include the input parameters used in its calculations and an explanation of how data gaps for the remaining category members will be addressed.

After careful, in-depth review, including contacting outside experts, the Testing Group decided that the use of the EQC Level III model suggested by EPA for evaluating the transport and distribution behavior of petroleum mixtures is at this time, an inappropriate approach. The Testing Group continues to support the use of a Level I fugacity calculation. The Testing Group reached this conclusion due to the lack of accurate emissions data and limitations of the algorithms, which require input of chemical specific properties. Furthermore, expert modeling scientists from the Center for Environmental Modeling, Trent University, Toronto, Canada have stated that Level 3 fugacity predictions are inappropriate for complex mixtures. Petroleum substances are, with minimal exception, characterized as complex, heterogeneous mixtures consisting of chemicals from different alkyl and aryl hydrocarbon classes. Due to the variability in hydrocarbon number and hydrocarbon type for the petroleum constituents, representative hydrocarbons were selected to predict potential partitioning behavior using simple Level I multimedia modeling equations.

The appropriate sections in the test plan and robust summary have been revised to include additional information and clarification on model input parameters as well as discussion on other category members.

<u>Ecological Effects</u>

For several of the ecological endpoints, EPA noted that it could not evaluate the reliability of toxicity values presented in a "Remark" section of the robust summary. Before the data could be used to satisfy an endpoint, the Agency felt the robust summary needed to be revised to include additional details of the studies from which the toxicity values were obtained.

The data cited in the "Remark" section within the robust summary for the ecotoxicity endpoints were intended only to provide supporting evidence to the primary study, which is

summarized in detail and satisfies the SIDS endpoints. These data were identified as such in the robust summary. It is the Testing Group's understanding that it is not necessary to provide detailed summaries for each individual study as long as one reliable study is described in detail and the supporting data represent the overall range of effects data found for the endpoint. This was reconfirmed during a meeting between API and EPA representatives on September 24, 2003.

With regard to fish, EPA commented that additional testing appeared to be needed for unrefined distillate base oils since no data on this subcategory were provided in the test plan. The Agency could not judge the adequacy of the studies performed on residual base oils and requested robust summaries be developed.

The Testing Group continues to believe that no additional testing is needed for this endpoint. The robust summary has been revised to describe a detailed reliable study for each subcategory of lubricating oil basestocks with supporting data provided in a "Remarks" section. Where a reliable study is lacking for a subcategory, additional discussion and/or data describing the toxicity relationships across subcategories within the lubricating oil basestocks category for similar HPV petroleum products has been provided.

EPA recommended additional toxicity testing of invertebrate and algae for both the unrefined distillate base oils and residual base oils categories.

The Testing Group continues to believe that no additional testing is needed for this endpoint. The robust summary has been revised to describe a detailed reliable study for each subcategory of lubricating oil basestocks with supporting data provided in a "Remarks" section. Where a reliable study is lacking for a subcategory, additional discussion and/or data describing the toxicity relationships across subcategories within the Lubricating Oil Basestocks category for similar HPV petroleum products has been provided.

EPA noted that the robust summary of the chronic toxicity studies on invertebrates did not contain analytical results that provided definitive evidence of stability of the test preparations.

For some studies, the study report states that samples were collected and stored for future analysis. Whether this analysis was done was not indicated in the report. When analyses of test solutions were made, the method employed total organic carbon measurements, which is not specific for the test substance and does not differentiate hydrocarbon types.

<u>Health Effects</u>

PETA took issue with the Testing Group's plan to perform additional selected toxicity testing on some of the category members.

The Testing Group shares PETA's goal that the HPV Challenge Program be conducted in a manner that takes into account animal welfare concerns. In this regard, the Testing Group also shares PETA's desire to limit the amount of toxicity testing which is performed under this test plan. However, the Testing Group continues to believe that the proposed testing is necessary to further characterize the SIDS level I mammalian toxicity of materials within the lubricating basestocks category.

With regard to mutagenic and carcinogenic potential of the distillate base oils, the Testing Group agrees with PETA that the PNAs are the "primary identified toxic compounds in the HPV test category". While the Testing Group believes a similar relation exists between PNA content and potential reproductive and development toxicity, the existing database is not as robust as that which exists for carcinogenicity/mutagenicity. Given the seriousness of this endpoint, the

Testing Group believes it is only prudent to evaluate this correlation by performing the reproductive/developmental screening tests proposed in the test plan. The Testing Group thinks the proposed testing will provide additional data to evaluate whether the correlation of PNA content and toxicity can be extended to include endpoints such as reproductive/developmental.

The Testing Group continues to favor not including the Unrefined/Mildly Refined oils in these reproductive/developmental screening tests, as we feel that the potential adverse reproductive/developmental effects of this subcategory are characterized by the results on a similar material, heavy vacuum gas oil.

The Testing Group agrees with PETA that the materials in all of the API HPV Testing Plans comprise a broad continuum. Viewing its various categories in this manner allows the API HPV Consortium to maximize the use of existing information and minimize the number of proposed tests. However, the existing data on the thirteen API HPV categories also illustrate the fact that there can be significant differences in toxicities within a single category and between different categories. These reported differences in toxicities have been one of the reasons that the Testing Group has proposed testing of selected lubricating basestocks.

ED suggested that footnote number 3 in Table 3, “Matrix of Available Data” should state "read across from Highly and Severely Refined Oils".

Footnote number 3 was correct. The Testing Group was planning to read across the carcinogenicity and *in vitro* mutagenicity studies on residual oils to the *in vivo* mutagenicity endpoint on residual oils. However, the Testing Group has decided to eliminate this “read across” and instead perform an *in vivo* mammalian erythrocyte micronucleus test (OECD 474) of a residual oil. The micronucleus test will be included in the 28 day repeat dose study on residual oil (see “Repeated Dose Toxicity” section). Given the negative results seen in *in vitro* genotoxicity and carcinogenicity studies and the lack of bioavailability of the very large and complex chemical species found in residual base oils (see “category justification” response), the Testing Group expects the results of the *in vivo* micronucleus test will be negative. While the Testing Group shares the desire to limit animal testing, the performance of the *in vivo* genotoxicity study will allow the Testing Group to confirm its hypothesis that the *in vivo* genotoxicity results will be negative.

ED thought the last 160 pages of the Robust Summary were redundant and unnecessary.

The Testing Group agrees with the ED comment. The Robust Summary the Testing Group submitted for posting was 85 pages. Unfortunately, the IUCLID export file the Testing Group also submitted was appended to the robust summary file before it was posted, resulting in a document 246 pages long. The Testing Group is including in this response a revised robust summary in which the IUCLID export file has been deleted.

At several points in its comments, EPA asked the Testing Group to justify the use of existing data from studies conducted via the dermal route of exposure. The Agency also asked for a similar justification with regard to why the proposed toxicity studies should be conducted via the dermal route, as opposed to the oral route.

The Testing Group is proposing to perform the mammalian toxicity tests via routes it considers to be primary routes of human exposure. This facilitates using the experimental data in human hazard and risk assessments. The Testing Group believes the dermal route of exposure has been and is appropriate for toxicity studies of this category of materials. This position is based on the following:

- **the dermal route is a likely route of human exposure,**
- **systemic effects have been seen in numerous studies of petroleum hydrocarbons done using the dermal route of exposure (including the developmental study on heavy vacuum gas oil summarized in this Test Plan),**
- **published data shows good absorption of PACs via both the dermal and oral routes of exposure in the rat, and**
- **the dermal route of exposure may minimizes the potential "first pass" metabolism by the liver of the biologically available/active impurities**.

Due to their physical nature (highly viscous), the dermal route is a primary route of human exposure to residual oils. Accordingly, the Testing Group continues to think the dermal route of exposure should be used in the toxicity study of residual base oil.

However, human exposure to highly/severely refined distillate oils can be through both oral and dermal routes. Therefore, the Testing Group agrees with EPA's suggestion that the reproductive/developmental screening toxicity study on a sample of a highly/severely refined distillate oil be conducted via the oral route of exposure.

EPA thought the *in vitro* genotoxicity studies included in the Test Plan/Robust Summary were inadequate since only one bacterial strain (TA 98) was tested. Furthermore, the data provided from the secondary source were too limited to address the chromosomal aberration endpoint. Consequently, EPA recommended genetic toxicity studies following OECD Test Guidelines 471 and 473 be conducted on selected category members.

Based on the substantive body of published data and acceptance by ASTM, the Testing Group does not consider it necessary to perform additional Ames tests with *Salmonella* strains of less or no sensitivity to hydrocarbon mutagenicity.

The standard Ames *Salmonella* Assay has been demonstrated to be inadequate for testing mineral oils that are extremely complex, water-insoluble mixtures (MacGregor et al., 1982: Cragg et al., 1985). To address these assay limitations, the Modified Ames Test was developed (Blackburn et al., 1984). This assay combines extraction of the oils with dimethyl sulfoxide to provide an aqueous-compatible hydrocarbon subfraction, and uses an eight-fold higher concentration of liver S-9 to increase the effective concentration of metabolically activated mutagenic species. Early studies demonstrated that of the 5 standard *Salmonella* strains employed by Ames, TA98 and TA100 gave positive results with extracted hydrocarbons, and that TA98 was the most sensitive of the strains for hydrocarbon mutagens (Hermann et al, 1980).

Results of studies testing complex hydrocarbons in TA98 have shown a strong correlation between mutagenicity in this strain and 3-7 ring PAC content, and with skin cancer in mice (Blackburn et al., 1986; Roy et al., 1988). The method has been patented (Blackburn et al., 1985) and approved by ASTM as a standard test method for base oils (ASTM E-1687-95) after an extensive round-robin evaluation procedure.

Regarding EPA's request for additional data on the chromosomal aberration endpoint included in the Robust Summary, the Testing Group has obtained copies of the laboratory reports from which the summary paper by Conaway et al. was generated. The Robust Summary has been revised to include additional data from these study reports. The Testing Group believes the revised Robust Summary includes sufficient information to address the chromosomal aberration endpoint. Consequently the Testing Group does not believe additional chromosomal aberration toxicity studies are needed.

Subcategory Specific Health Comments

Unrefined/mildly refined distillate base oils
EPA requested the Testing Group provide more details in the robust summary on the repeated-dose toxicity study of heavy vacuum gas oil (HVGO), an analog of the unrefined distillate base oil category.

The Robust Summary has been revised to include additional experimental details. The Testing Group believes these details will allow readers to assess the adequacy of and support the use of data from the HVGO study to assess the repeat dose and reproductive/developmental toxicity of the unrefined/mildly refined distillate oils. Consequently, the Testing Group does not anticipate it will need to conduct (per EPA's suggestion) a combined repeated-dose/reproductive/developmental toxicity screening test on an unrefined/mildly refined base oil.

ED thought the Test Plan needed to include additional information regarding the Testing Group's assertion that heavy vacuum gas oil was an analog for the unrefined/mildly refined distillate base oil category. Even if additional information is provided, ED recommended the reproductive/developmental testing of an unrefined/mildly refined oil.

Additional discussion has been added to the Test Plan regarding the relationship of heavy vacuum gas oils (HVGO) and unrefined and mildly refined oils. Given its physical and compositional similarities to distillate base oils, HVGO could have been included in this category. However, because it is primarily used in fuel oil processing, the Testing Group decided to include HVGO in the Heavy Fuel Oils HPV Test Plan.

The Testing Group believes additional reproductive/developmental toxicity testing of the unrefined/mildly refined distillate oils is unnecessary. The Testing Group reached this conclusion after reviewing data from two studies on HVGO, a developmental screen and a 90-day repeat-dose study in which sperm morphology was examined. The Testing Group, continues to believe the data from these two studies is sufficient to characterize the reproductive/developmental toxicities of the unrefined/mildly refined distillate oils. Since the unrefined/mildly refined distillate oils contain similar or fewer levels of potentially toxic impurities, the use of the HVGO data might err by overestimating the potential toxicity of the unrefined/mildly refined se materials.

Highly/Severely refined distillate base oils
EPA requested additional justification to support the use of the 90-day oral study on a food grade white oil to represent the highly refined base oils subcategory. The Agency did note that in lieu of the additional justification, a 4-week inhalation repeated-dose toxicity study of three base oils (two of which were highly/severely refined non-food grade oils) may provide adequate data on a highly refined material (not food grade); but study details were missing from the robust summary.

The Testing Group thinks the 90-day study on the food grade white oil is of value since it defines the upper boundary of the highly/severely refined oils subcategory. However, the Testing Group agrees with EPA that the lower range of that subcategory is better represented by highly/severely refined non-food grade oils, similar to two of the three materials used in the 4-week inhalation study. Therefore, per the Agency's request, the robust summary has been revised to include the requested details on the 4-week inhalation repeated dose study on highly/severely refined base oils.

EPA commented that the submitted dermal studies of the highly/severely refined distillate oils were inadequate because they used a 3-day-per-week dosing schedule.

While acknowledging that the OECD guidelines for dermal toxicity call for daily administration of the test substance, The Testing Group disagrees with EPA's assessment of the adequacy of the dermal studies. The petroleum industry's extensive experience in testing petroleum hydrocarbons has shown many of them are capable of producing extreme dermal irritation when administered repeatedly (i.e. on a daily basis). Dilution of the test material and lower doses are methods that can be used to reduce the dermal irritation that a test material produces. However, both methods raise technical issues with regard to interpreting test results. The modification of the dermal test protocol to application of test material to 2 or 3 times per week was successful in allowing the application in chronic animal studies of large weekly doses, with minimal dermal irritation. The tested doses exceeded 1000 mg/kg$_{bw}$ weekly in the chronic animal studies, a dose that exceeds the recommended current maximum guidelines. The Testing Group notes that this dosing regime of 2-3 times per week is a technique that has been used successfully in the majority of dermal toxicity studies performed on petroleum hydrocarbons.

In addition to the proposed reproductive/developmental screening study (OECD 421) of a highly/ severely refined distillate base oil, ED suggested that the Testing Group perform a similar study on a less refined stream.

The Testing Group notes that the reproductive/developmental toxicity of the less refined streams (unrefined/mildly refined) will be read across from an existing study on heavy vacuum gas oil.

Residual base oils

EPA asked the Testing Group to specify the residual base oil that would be tested in the repeat dose/reproduction/developmental screening study.

The Testing Group agrees with EPA that the sample selected for testing should be potentially the most toxic. For this reason, the Testing Group intends to test a sample of de-asphalted

residual oil, an oil that has received a minimum amount of processing. De-asphalted residual oils have had resins and asphaltenes removed, but still contain relatively high (maximum) levels of other impurities, including aromatic hydrocarbons.

ED suggested the proposed repeat-dose study of the residual base oils be incorporated via a combined testing protocol into the proposed Repro/Developmental study of this material.

The Testing Group appreciates the ED suggestion to combine the two studies. The current Test Plan calls for performing such a combined study, a repeat-dose/reproductive/ developmental screening study (OECD 422).

The Testing Group appreciates the comments and interest by all stakeholders in the Lubricating Basestocks testing program. We believe that the revised Test Plan and Robust Summary, submitted via this letter, are both scientifically sound and meet the spirit of the EPA's guidance on animal welfare. The revised Test Plan makes every effort to minimize the number of animals used in toxicity testing, while at the same time allowing the sponsors to fulfill their product stewardship responsibilities under the High Production Volume Challenge Program.

If you have further questions or comments about the program, please call me at (202) 682-8344, or Tom Gray at (202) 682-8480.

Sincerely,

Lorraine E. Twerdok, Ph.D, D.A.B.T.
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Attachment: References

References

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